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(FILE 'USPAT' ENTERED AT 09:46:55 ON 24 JAN 95)

E GARNER IAN/IN
E GARNER, IAN/IN
E DALRYMPLE, MICHAEL L/IN
E PRUNKARD, DONNA E/IN
E FOSTER, DONALD C/IN

L1	7	S	E3
L2	304	S	TRANSGEN?
L3	3056	S	FIBRINO?
L4	117224	S	HUMAN
L5	37	S	ZYMOGENETICS/ASN
L6	0	S	L2 (P) L3
L7	1763	S	MAMMARY
L8	18	S	L2 (P) L7
L9	0	S	L8 AND L5
L10	7	S	L2 AND L3
L11	305	S	L3 (A) L4
L12	3	S	L11 (P) (CDNA OR GENE)

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U.S. Patent & Trademark Office LOGOFF AT 09:55:56 ON 24 JAN 95

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3070 W4[illegible]
NO CARRIER

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     (FILE 'HOME' ENTERED AT 09:24:29 ON 24 JAN 95)

     FILE 'CA' ENTERED AT 09:24:35 ON 24 JAN 95
                E GARNER I/AU
L1           28 S E3-E5
                E DALRYMPLE ML/AU
                E DALRYMPLE MICHAEL L/AU
                E DALRYMPLE M L/AU
                E PRUNKARD D/AU
L2            4 S E4-E5
                E FOSTER D C/AU
L3            2 S E3
                E FOSTER DONALD C/AU
L4           30 S E3-E4
                E FOSTER DC/AU
L5           64 S L1-L4
L6        14301 S FIBRINOG?
L7            0 S L5 AND L6
L8         8997 S TRANSGEN?
L9            3 S L5 AND L8
L10           0 S L6 AND L7
L11        1945 S L6 AND BETA
L12         121 S L6 (A) BETA
L13         253 S L6 (A) GAMMA
L14         229 S L6 (A) ALPHA
L15         558 S L12-L14
L16          39 S L15 AND RECOMB?
L17        1256 S L6 (A) HUMAN
L18          29 S L17 AND CDNA
L19           5 S L17 (3A) CDNA
L20           4 S ZEM228
L21           2 S ZEM219B
L22         256 S L8 AND MAMMARY
L23        2373 S LACTOGLOBULIN
L24       25570 S CASEIN
L25        2593 S LACTALBUMIN
L26         288 S (L22-L25) (2A) PROMOTER#
L27         115 S L26 AND L22
L28          23 S L22 AND LACTOGLOBULIN

     FILE 'BIOSIS' ENTERED AT 09:44:21 ON 24 JAN 95
L29          18 S L28

=) loy y
'LOY' IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=).

=) log y
COST IN U.S. DOLLARS                          SINCE FILE      TOTAL
                                                 ENTRY    SESSION
FULL ESTIMATED COST                              10.46     118.52

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)    SINCE FILE      TOTAL
                                                 ENTRY    SESSION
CA SUBSCRIBER PRICE                               0.00     -13.00
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116:122167 High level expression of active human alpha-1-antitrypsin in the milk of ***transgenic*** sheep. Wright, G.; Carver, A.; Cottom, D.; Reeves, D.; Scott, A.; Simons, P.; Wilmut, I.; ***Garner, I.*** ; Colman, A. (Pharm. Proteins Ltd., Edinburgh, EH9 3JQ, UK). Bio/Technology, 9(9), 830-4 (English) 1991. CODEN: BTCHDA. ISSN: 0733-222X.

AB The generation of 5 sheep ***transgenic*** for a fusion of the ovine .beta.-lactoglobulin gene promoter to the human .alpha.1-antitrypsin (h.alpha.1AT) genomic sequences is described. Four of these animals are female and 1 male. Anal. of the expression of h.alpha.1AT in the milk of 3 of these females shows that all express the human protein at levels greater than 1 g per L. In one case initial levels exceeded 60 g/L and stabilized at approx. 35 g/L as lactation progressed. Human .alpha.1AT purified from the milk of these animals appears to be fully N-glycosylated and has a biol. activity indistinguishable from human plasma-derived material.

L16 ANSWER 15 OF 39 CA COPYRIGHT 1995 ACS

115:202768 ***Recombinant*** production, secretion, and clotting behavior of fibrinogen, and cell line used therein. Redman, C.; Samar, R. (United States Dept. of Health and Human Services, USA). U. S. Pat. Appl. US 663380 A0 910901, 32 pp. Avail. NTIS Order No. PAT-APPL-7-663 380. (English). CODEN: XAXXAV. APPLICATION: US 91-663380 910304.

AB A method is provided for fibrinogen prodn. comprising introduction into a cell of a ***recombinant*** DNA mol. (or mols.) encoding the (preferably human) B.alpha., B.beta., and . ***gamma*** . ***fibrinogen*** subunits, then effecting expression of the DNA mol(s). under conditions such that the fibrinogen subunits are assembled into a fibrinogen mol. The fibrinogen mol. is preferably secreted from the cell and is capable of forming a thrombin-induced clot. Fibrinogen-producing cells are also provided. Construction of expression vectors for fibrinogen subunit prodn. is described, as is transfection of COS cells with the vectors and prodn. of single and combinations of fibrinogen chains. COS cells which expressed single fibrinogen chains, and those which expressed 2 of the chains, did not secrete these proteins into the medium. COS-.alpha.,.beta.,.gamma. cells expressed and secreted the proteins into the medium. Under nonreducing conditions, the secreted fibrinogen chains were components of a high-mol.-wt. (340,000) disulfide-linked complex; no free fibrinogen chains or intermediate products of assembly were detected in the medium. In 2 expts., 2 .times. 106 COS-.alpha.,.beta.,.gamma. cells secreted an av. of 2.08 .mu.g fibrinogen/24 h. The clotting behavior of the ***recombinant*** fibrinogen is described, as is endoglycosidase-H sensitivity of nonsecreted chains.

L16 ANSWER 17 OF 39 CA COPYRIGHT 1995 ACS

115:155812 ***Recombinant*** human fibrinogen and sulfation of the .gamma.' chain. Farrell, David H.; Mulvihill, Eileen P.; Huang, Shaoming; Chung, Dominic W.; Davie, Earl W. (Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA). Biochemistry, 30(39), 9414-20 (English) 1991. CODEN: BICHAW. ISSN: 0006-2960. OTHER SOURCES: CJACS.

AB Human fibrinogen and the homodimeric .gamma.'-chain-conto. variant were expressed in BHK cells using cDNAs coding for the .alpha., .beta., and .gamma. (or .gamma.') chains. The fibrinogens were secreted at levels >4 .mu.g (mg of total cell protein)-1 day-1 and were biol. active in clotting assays. ***Recombinant***

fibrinogen contg. the .gamma.' chain incorporated 35S04 into its

chains during biosynthesis, while no incorporation occurred in the protein contg. the .gamma. chain. The identity of the sulfated .gamma.' chain was verified by its ability to form dimers during clotting. In addn., carboxypeptidase Y digestion of the ***recombinant*** fibrinogen contg. the .gamma.' chain released 96% of the 35S label from the sulfated chain, and the radioactive material was identified as tyrosine O-sulfate. These results clarify previous findings of the sulfation of tyrosine in human fibrinogen.

L16 ANSWER 31 OF 39 CA COPYRIGHT 1995 ACS

106:150584 Characterization of the 5'-flanking region for the human ***fibrinogen*** . ***beta*** . gene. Huber, Philippe; Dalson, Jacques; Courtois, Gilles; Laurent, Monique; Assouline, Zahra; Marguerie, Gerard (Lab. Hematol., INSERM, Grenoble, F 38041, Fr.). Nucleic Acids Res., 15(4), 1615-25 (English) 1987. CODEN: NARHAD. ISSN: 0305-1048.

AB To identify the possible regulatory sequences in the genetic expression of fibrinogen, a human genomic DNA library raised in .lambda.EMBL 4 phage was screened using cDNA probes coding for the A.alpha., B.beta., and .gamma. chains of human fibrinogen. The entire fibrinogen locus was characterized and its organization analyzed by means of hybridization and restriction mapping. Among the clones identified, a single ***recombinant*** .lambda. phage contained the .beta. gene and its 5'- and 3'-flanking regions. A 1.5-kb fragment of the intermediate 5'-flanking region was sequenced and S1 mapping expts. revealed 3 transcription start points. Comparison of this sequence with that previously reported for the same region upstream from the human .lambda. gene revealed no significant homol., which suggests that the potential promoting sequences of these genes are different. In contrast, comparison of the 5'-flanking regions of human and rat .beta. genes revealed a 142-bp sequence of 80% homol. situated 16-bp upstream from the human .beta. gene. This highly conserved region may well represent a potential candidate for a regulatory sequence of the human .beta. gene.

L16 ANSWER 35 OF 39 CA COPYRIGHT 1995 ACS

99:153167 Cloning of fibrinogen genes and their cDNA. Chung, Dominic W.; Rixon, Mark W.; Que, Benito G.; Davie, Earl W. (Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA). Ann. N. Y. Acad. Sci., 408(Mol. Biol. Fibrinogen Fibrin), 449-56 (English) 1983. CODEN: ANYAA9. ISSN: 0077-8923.

AB The gene for the .beta.-chain of human fibrinogen was seqd. from a human genomic DNA library with radiolabeled cDNA for a bovine ***fibrinogen*** . ***beta*** .-chain gene. The overall homol. of this probe with human .beta.-chain fibrinogen is .apprx.75%. Seven of 2 .times. 106 ***recombinant*** phages hybridized specifically with the probe. DNA was extd. and analyzed by restriction endonuclease mapping and Southern hybridization. Electron microscopic heteroduplex mapping of the .beta.-chain gave size ests. of the 7 intervening sequences (introns) and 8 exons. The gene was further characterized, after cloning in pBR322, by restriction endonuclease mapping and nucleotide sequencing. The positions at which several introns interrupt the coding regions appear to be related to the functional domains of the polypeptide. Over 65% of the gene sequence was deld., and a putative signal peptide was identified.

L16 ANSWER 36 OF 39 CA COPYRIGHT 1995 ACS

99:17449 Characterization of a complementary deoxyribonucleic acid coding for the .gamma. chain of human fibrinogen. Chung, Dominic W.; Chan, Wai Yee; Davie, Earl W. (Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA). Biochemistry, 22(13), 3250-6 (English) 1983. CODEN: BICHAW. ISSN: 0006-2960. OTHER SOURCES: CJACS.

AB A no. of cDNAs that encode the .gamma. chain of human fibrinogen were isolated from a liver cDNA library by employing a synthetic nucleotide mixt. as a probe. One of the pos. clones was then used to screen the entire cDNA library of 18,000 ***recombinants*** : this screening yielded 320 pos. clones for the .gamma. chain. The largest cDNA was 1638 base pairs and contained 10 base pairs of p(oly(G) at the 5' end, which were followed by 71 base pairs of noncoding nucleotides. The next 78 base pairs coded for a leader sequence of 26 amino acids and included a methionine start signal and a typical hydrophobic core. The following 1233 base pairs coded for 411 amino acids that are {present in the mature protein; these were followed by a stop codon of TAA. 207 base pairs of noncoding nucleotides, a poly(A) track of 15 base pairs, and 22 base pairs of poly(C). Specific regions of the cDNA of the .gamma. chain were then compared with the cDNAs for the .alpha. and .beta. chains of human fibrinogen.

L16 ANSWER 37 OF 39 CA COPYRIGHT 1995 ACS

99:17447 Characterization of a complementary deoxyribonucleic acid coding for the .alpha. chain of human fibrinogen. Rixon, Mark W.; Chan, Wai Yee; Davie, Earl W.; Chung, Dominic W. (Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA). Biochemistry, 22(13), 3237-44 (English) 1983. CODEN: BICHAW. ISSN: 0006-2960. OTHER SOURCES: CJACS.

AB A human liver cDNA library was screened for the .alpha. chain of fibrinogen with a cDNA clone from the corresponding bovine mol. as a hybridization probe. Several human clones coding for the .alpha. chain were identified, and 1 of these was used to rescreen the entire cDNA library of 18,000 ***recombinants*** . Plasmids with the largest cDNAs were isolated, and their inserts were sequenced. The largest cDNA insert contained 2224 base pairs, including a noncoding region at the 5' end that was followed by a region coding for a signal peptide of 19 (or 16) amino acids and a mature protein of 625 amino acids, a stop codon of TAG, another noncoding region, and a poly(A) tail at the 3' end. Eight tandem repeats of 39 base pairs were obsd. which started with nucleotide 985 (amino acid residue 270) and ended with nucleotide 1213 (amino acid residue 372). The identity in the nucleotide sequence in the tandem repeats ranged 72-95% when compared to a consensus sequence. The predicted amino acid sequence for the mature polypeptide chain was 15 amino acids longer at the C-terminal end than that of the .alpha. chain isolated from plasma fibrinogen and sequenced. Apparently, minor proteolysis of the C-terminus of the .alpha. chains had occurred, probably during secretion or circulation of the protein in plasma.

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119:179358 Manufacture of thrombin analogs in transgenic animal and yeast cells. Holly, Richard D.; Foster, Donald C. (Zymogenetics, Inc., USA). PCT Int. Appl. WO 9313208 A1 930708, 78 pp. DESIGNATED STATES: W: AU, CA, FI, JP, NO; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (Engli[redacted] CODEN: PIXXD2. APPLICATION: WO 92-US11357 921230. PRI[redacted]: US 91-816281 911231; US 92-860701 920331.

AB Thrombin analogs lacking the pla domain are manufd. for therapeutic

use by expression of the corresponding genes in animal cell and

yeast systems. A human prothrombin cDNA was cloned from a liver bank and cDNAs for analogs lacking the ula domain constructed by std. methods. The deletion analog cDNA was placed under control of SV40 regulatory elements and the signal sequence of a human tissue plasminogen activator gene used to direct secretion of the product. BHK570 cells transformed with these constructs yielded 3.4-20 .mu.g thrombin/mL medium. Expression systems for animal cells using a signal sequence for a peptide cleavable by the KEX2 proteinase of Saccharomyces cerevisiae and the KEX2 gene were also constructed. A similar system was constructed for use of S. cerevisiae as expression host.

120:126149 An animal cell line stably expressing a glutamate receptor gene. Andersen, Peter Hoengaard; Rasmussen, Jesper Skou; Stidsen, Carsten E.; Nielsen, Lars Soegaard (Novo Nordisk A/S, Den.). PCT Int. Appl. WO 9324629 A1 931209, 25 pp. DESIGNATED STATES: W: JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 93-DK169 930519. PRIORITY: DK 92-685 920525.

AB Mammalian cells transfected with a DNA sequence encoding a protein with electrophysiol. and pharmacol. properties characteristic of a glutamate receptor, or a functional fragment of the receptor and capable of permanently expressing said DNA sequence are established. BHK570 cells were found to stably present a significant quisqualate-insensitive glutamate-binding activity that may play a role in the stability of the receptor. A cDNA for an AMPA-binding glutamate receptor of rat hippocampus or cerebellum was cloned by RT/PCR and cloned into the mammalian expression vector ***Zem219b*** for transfection into BHK570 cells. Transformants showed a pharmacol. consistent with the presence of a flip receptor.

117:169549 Production of human .alpha.1-antitrypsin in the milk of ***transgenic*** sheep and mice: targeting expression of cDNA sequences to the ***mammary*** gland. McClenaghan, M.; Archibald, A. L.; Harris, S.; Simons, J. P.; Whitelaw, C. B. A.; Wilmut, I.; Clark, A. J. (Inst. Anim. Physiol. Genet., AFRC, Roslin/Midlothian, EH25 9PS, UK). Anim. Biotechnol., 2(2). 161-76 (English) 1991. CODEN: ANBTEN. ISSN: 1049-5398.

117:105316 Targeting expression to the ***mammary*** gland: intronic sequences can enhance the efficiency of gene expression in ***transgenic*** mice. Whitelaw, C. Bruce A.; Archibald, Alan L.; Harris, Stephen; McClenaghan, Margaret; Simons, J. Paul; Clark, A. John (Inst. Anim. Physiol. Genet., AFRC, Roslin/Midlothian, EH25 9PS, UK). Transgenic Res., 1(1). 3-13 (English) 1991. CODEN: TRSEES.

111:110001 Expression of human anti-hemophilic factor IX in the milk of ***transgenic*** sheep. Clark, A. J.; Bessos, H.; Bishop, J. O.; Brown, P.; Harris, S.; Lathe, R.; McClenaghan, M.; Prowse, C.; Simons, J. P.; et al. (Inst. Anim. Physiol. Genet. Res., AFRC, Edinburgh, EH9 3JQ, UK). Bio/Technology, 7(5). 487-92 (English) 1989. CODEN: BTCHDA. ISSN: 0733-222X.

L28 ANSWER 22 OF 23 CA COPYRIGHT 1995 ACS

109:223892 Gene transfer into sheep. Simons, J. Paul; Wilmut, Ian; Clark, A. John; Archibald, Alan L.; Bishop, John O.; Lathe, Richard (Inst. An113:113782 High-level expression of biologically active human .alpha.1-antitrypsin in the milk of ***transgenic*** mice.

Archibald, Alan L.; McClenaghan, Margaret; Hornsey, Valerie; Simons,

J. Paul; Clark, A. John (Inst. Anim. Physiol. Genet. Res., AFRC, Roslin/Midlothian, EH25 9PS, UK). Proc. Natl. Acad. Sci. U. S. A., 87(13), 5178-82 (English) 1990. CODEN: PNASA6. ISSN: 0027-8424.

L28 ANSWER 20 OF 23 CA COPYRIGHT 1995 ACS
113:56187 Gene expression in the ***mammary*** gland. Harris, S.; McClenaghan, M.; Simons, J. P.; Ali, S.; Clark, A. J. (Inst. Anim. Physiol. Genet. Res., AFRC, Roslin/Midlothian, EH25 9PS, UK). J. Reprod. Fertil., 88(2), 707-15 (English) 1990. CODEN: JRPFA4. ISSN: 0022-4251.

L28 ANSWER 21 OF 23 CA COPYRIGHT 1995 ACS
111:110001 Expression of human anti-hemophilic factor IX in the milk of ***transgenic*** sheep. Clark, A. J.; Bessos, H.; Bishop, J. O.; Brown, P.; Harris, S.; Lathe, R.; McClenaghan, M.; Prowse, C.; Simons, J. P.; et al. (Inst. Anim. Physiol. Genet. Res., AFRC, Edinburgh, EH9 3JQ, UK). Bio/Technology, 7(5), 487-92 (English) 1989. CODEN: BTCHDA. ISSN: 0733-222X.

L28 ANSWER 22 OF 23 CA COPYRIGHT 1995 ACS
109:223892 Gene transfer into sheep. Simons, J. Paul; Wilmut, Ian; Clark, A. John; Archibald, Alan L.; Bishop, John O.; Lathe, Richard (Inst. Anim. Physiol. Genet. Res., AFRC, Edinburgh, EH9 3JQ, UK). Bio/Technology, 6(2), 179-83 (English) 1988. CODEN: BTCHDA. ISSN: 0733-222X.

92:233597 Document No.: BA93:121622. INDUCTION OF LACTOGENESIS IN ***TRANSGENIC*** VIRGIN PIGS EVIDENCE FOR GENE AND INTEGRATION SITE-SPECIFIC HORMONAL REGULATION. SHAMAY A; PURSEL V G; HALL R J; HENNIGHAUSEN L. NATIONAL INST. HEALTH, BUILDING 10, ROOM 9N113, BETHESDA, MD. 20892. MOL ENDOCRINOL, 6 (2). 1992. 191-197. CODEN: MOENEN; ISSN: 0888-8809. Language: English

L29 ANSWER 12 OF 16 BIOSIS COPYRIGHT 1995 BIOSIS
92:194662 Document No.: BA93:105612. PRODUCTION OF HUMAN ALPHA-1 ANTITRYPSIN IN THE MILK OF ***TRANSGENIC*** SHEEP AND MICE TARGETING EXPRESSION OF CDNA SEQUENCES TO THE ***MAMMARY*** GLAND. MCCLENAGHAN M; ARCHIBALD A L; HARRIS S; SIMONS J P; WHITELAW C B A; WILMUT I; CLARK A J. AFRC INST. ANIMAL PHYSIOL. GENETICS, EDINBURGH RESEARCH STATION, ROSLIN, MIDLOTHIAN, SCOTLAND EH25 9PS. ANIM BIOTECHNOL, 2 (2). 1991. 161-176. CODEN: ANBTEN; ISSN: 1049-5398. Language: English